REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. AGENCY USE ONLY *(Leave blank)*	2. REPORT DATE 05/09/2002	3. REPORT TYPE AND DATES COVERED Final Technical Report

4. TITLE AND SUBTITLE
NEURAL CONTROLLER FOR AN ARTIFICIAL LIMB: DEVELOPMENT OF A BIO/ROBOTIC INTERFACE

5. FUNDING NUMBERS
G N00014-97-1-0714

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8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)
Office of Naval Research

10. SPONSORING/MONITORING AGENCY REPORT NUMBER

11. SUPPLEMENTARY NOTES

12a. DISTRIBUTION/AVAILABILITY STATEMENT
Distribution Unlimited

20020621 080

13. ABSTRACT *(Maximum 200 words)*
This AASERT project was aimed at complementing an ongoing research project funded by ONR (grant n. N00014-95-1-0571). The goal of the parent grant was twofold: a) to further our understanding of the organization of motor control in the spinal cord and b) to develop an artificial system consistent with this understanding. The purpose of this augmentation award was to enhance the ongoing sponsored research while training a graduate student in Mechanical Engineering.
The system developed thanks to the AASERT support is a hybrid device that combines living neural tissue from the sea Lamprey brainstem and spinal cord with a small mobile robot. The goal was therefore twofold: 1) developing a novel device and 2) engaging a graduate student in an advance research/development project. The AASERT award has provided an extremely valuable complement of the parent grant. The research under the AASERT award led to a novel and successful line of research, aimed at the integration of living neural tissue with artificial devices. This goal has been reached and the first prototype of a hybrid system operating with a closed sensory-motor loop has been created and utilized for investigating the structure of the neural connections and the mechanisms of synaptic plasticity.

14. SUBJECT TERMS	15. NUMBER OF PAGES 5
	16. PRICE CODE

17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
UNCLASSIFIED			UL

NSN 7540-01-280-5500 Computer Generated STANDARD FORM 298 (Rev 2-89)
Prescribed by ANSI Std 239-18
298-102

FINAL TECHNICAL REPORT

GRANT #: N00014-97-1-0714

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INSTITUTION: Northwestern University Medical School

GRANT TITLE: "NEURAL CONTROLLER FOR AN ARTIFICIAL LIMB: DEVELOPMENT OF A BIO/ROBOTIC INTERFACE,"

AWARD PERIOD: 6/1/97 – 5/31/00

OBJECTIVE:.
The goal of this AASERT project was to complement an ongoing research project funded by ONR (grant n. N00014-95-1-0571). The goal of the parent grant was twofold: a) to further our understanding of the organization of motor control in the spinal cord and b) to develop an artificial system consistent with this understanding. The purpose of this augmentation award was to enhance the ongoing sponsored research while training a graduate student in Mechanical Engineering.
The system developed thanks to the AASERT support is a hybrid device that combines living neural tissue from the sea Lamprey brainstem and spinal cord with a small mobile robot. The goal was therefore twofold: 1) developing a novel device and 2) engaging a graduate student in an advance research/development project.

APPROACH:
The AASERT student (Bernard Reger) participated in research activities aimed at developing an integrated system composed of a neuronal preparation and a robotic device in mutual interaction.
This research was an extension of the project entitled The organization of motor behavior by the combination of vector fields in biological and artificial control systems", which was supported by ONR grant N00014-95-1-0571 in the period 3/1/95 - 2/28/99. The ASSERT award actually developed the technical foundation for a second parent award entitled "Neurally guided robot navigation" (ONR grant N00014-99-1-0881).

The neural component of the hybrid system is a portion of the brainstem of the Sea Lamprey in its larval state. The whole brain of anesthetized larvae of Sea Lamprey was dissected and maintained in continuously superfused, oxygenated and refrigerated Ringer's Solution. The activity of neurons was recorded in the a region of the reticular formation, a relay that connects different sensory systems (visual, vestibular, tactile) and central commands to the motor centers of the spinal cord. Two recording electrodes were placed in the right and left Posterior Rhombencephalic Reticular Nuclei (PRRN). Two unipolar tungsten stimulation electrodes were placed among the axons of the Intermediate and Posterior Octavomotor nuclei (nOMI and nOMP). These nuclei receive inputs from the vestibular capsule and their axons form synapses with the Rhombencephalic neurons on both sides.
While the axons of the nOMI remain in the same side of the spinal cord where they originate, nOMP neurons cross the midline. As a result, the activity of one vestibular capsule affects reticulo spinal (RS) nuclei on both side of the midline. In order to elicit bilateral responses , stimulation electrodes were placed in the region where the axons of the nOMI and nOMP cross. This placement of the electrodes induced predominantly excitatory responses in the downstream neurons. The recording electrodes were placed on either side of the midline, near the visually identified neurons of the
PRRN.

In the early stages of this project, we planned to use an artificial two-joint limb as a robotic component. However, we soon modified our plans based on the analysis of the information processing that is naturally carried out by the Lamprey's brainstem. This neural structure coordinates signals that are directed to the right and left sides of the body. It receives sensory information from symmetric structures on the two sides and it also delivers motor commands to symmetric structures. This right/left symmetry is not reflected in the dynamics and kinematics of a robotic limb. However, a similar symmetry is evident in mobile robots, where the motion of wheels on the right and left sides is governed by information that originates from sensors on the two sides. Accordingly, a mobile robot - the base Khepera module manufactured by K-Team - was chosen as the artificial component to be interfaced with neural tissue. The small size of this system allowed us to design a small circular workspace (2 ft diameter). Placed along the circumference of the robot are eight sensors each nproviding proximity and light intensity information. Two wheels provide a means of locomotion for the small robot. A computer system communicates with the robot through the serial port and a custom designed LabVIEW application. Eight lights are mounted at the edge of the robot workspace at 45 degree intervals. The lights are computer controlled and generate the stimulus that elicit a phototactic response.

The brain/robot interface acts as an interpreter between the neural signals and the robot control system . It is responsible for the transformation of the robot's light sensor information into electrical stimuli and then for processing in real time the neural activity of the reticulo-spinal nuclei and forntranslating it into motor commands for the robot.

The light intensities detected by the robot sensors determine the frequencies at which the right and left vestibular pathways are stimulated. This system prototype makes a simple proportional translation from light intensity to stimulation frequency.

The spiking activities of the PRRN as recorded near the axons is analyzed through a five step process. The signal picked up by the recording electrodes contains a combination of spikes, stimulus artifacts, excitatory and inhibitory postsynaptic potentials and noise. To suppress the slow PSP components, this signal is first put through a high pass filter. The output of this filter contains high frequency noise, stimulus artifacts, and the spikes generated by multiple neurons in the vicinity of the electrode. Stimulus artifacts are canceled by zeroing the recorded signals over temporal following the delivery of each stimulation pulse. The remaining signal is rectified, and a threshold is applied to separate the spikes from the background noise. The resulting train of spikes, is put through a low pass filter (5 Hz) which effectively generates a rate coded signal. The mean of this signal is used for controlling each of the robot's wheels.

The experimental apparatus built under this award includes a system for the acquisition of robot movements. The robot position and orientation is sampled and acquired using an overhead color camera (Ultrak STC-630A). The image frames are acquired at a rate of 60Hz. Each frame is analyzed to determine the center and orientation of the robot. Trajectories induced by the same light stimulus can be quantitatively compared by a "figural distance" measure, which is based on the repeated measure of the Euclidean distance between each point in one trajectory and all the points in the other. The figural distance between two trajectories is a symmetric measure of the difference between the shapes of the respective paths. Figural distance proved to be an adequate measure for assessing stability of the neur-robotic system and for evaluating the degree of change in behavior induced by plastic modifications of synaptic transmission.

A distinctive feature of the system developed under this award is the possibility to interchange actual living tissue, with its computational simulation. This allows for a direct comparison of theoretical models with actual neuronal behavior. A simulation platfoprm has been developed, based on the interaction of three systems: a) the robot's motor system b) the robot sensory system and c) the lamprey's brain. The dynamics of the mobile robot are described by a system of three nonlinear first-order differential equations that relate the angular velocity of the wheels and the current position/orientation of the robot to the next

position/orientation of the robot. On the sensory side, the intensity signal generated by each sensor is inversely proportional to the square distance to the light source. With a fixed light source, this provides a relation between the state (position/orientation) of the robot and the resulting sensor signal.

Unlike the robot and its sensors, the operation of the brain is essentially unknown. One of the purposes of the hybrid system is actually to investigate the computational properties of this neural tissue. In a number of simulations, a simplified model of the neural system has been considered, with two inputs, two outputs and a bivariate polynomial relation between each output and the two inputs. In the simplest linear case, the outputs are proportional to the inputs via a ``weight matrix", W, whose elements may be taken to represent the strengths of the synaptic connections between stimulated axons and reticular neurons. Positive weights represents excitatory connections and negative weights inhibitory connections. When all the above components are assembled into a single system, one obtains differential equations in which the rate of change of the state vector depends only upon the state vector itself, and not on time.
The particular behaviors emerging from this autonomous system are determined by the parameters that describe the behavior of the neural system and that may be assumed to be time-invariant or, at least, to be varying on a time scale that is much longer than the scale of each behavior. The process of adaptation and synaptic plasticity are thus represented and evaluated by the changes in the weight matrix parameters or in the parameters that describe the input/output behavior of the neural tissue.

ACCOMPLISHMENTS

The AASERT award has accomplished two main objectives:

1) It enhanced the parent project and led to a new and exciting line of research on brain-robot interactions
2) It supported the successful training of a graduate student in Mechanical Engineering, Bernard D. Reger who obtained a PhD in June 2000 after presenting a dissertation entitled "A Neuro-Robotic Interface for the Study of Synaptic Plasticity in Sensorymotor Adaptation".

A concrete outcome of this study has been the creation of a prototype system in which a portion of neural tissue from the lamprey's reticular formation is connected through a computer interface with a mobile robot. The optical
sensors on the robot determine the parameters of the electrical stimuli delivered to the vestibular axons of the lamprey. The signals recorded from the neural populations with which these axons form synapses are used as control signals for the robot's movement. A distinctive feature of this system is that it exploits a closed-loop relation between the neural tissue and robot, which operates as an artificial body. The movements determined by activities in the reticular neurons cause changes in the robot's exposure to the light generated by a fixed source. These changes, in turn, cause a variation in the electrical stimulus that is responsible for the activities in the same reticular neurons. This paradigm is well suited for investigating the operation of Hebbian learning mechanisms by which the strength of a given synapse is modified based on the correlation between pre and postsynaptic activities.

It was found that, with some exceptions, the neuro-robotic system generated stable behaviors over extended periods of time. Stability was assessed by observing the repeatability of the trajectories triggered by light sources placed at different locations. Stability of the behaviors generated by our preparation is a necessary condition for proceeding with further analysis and, in particular, with investigations that assume that the neural connectivity remains invariant over the time scale of individual sensory-motor responses.
Different preparations of the neural tissue led to markedly different behaviors in response to the light. Among the observed behaviors are: light-seeking behaviors (positive phototaxis), light aversion behaviors (negative phototaxis) and linear combinations of light seeking and light aversion (mixed phototaxis). We found that a simple linear model is sufficient to account for these different types of behavior on the basis of the amount of ipsi- and contralateral connections between stimulating and recording electrodes.

Finally, in these studies we begun to observe systematic adaptive responses induced by the selective alteration of the sensor signals on one side of the robot. In particular, we have documented a strong alteration of behavior followed by gradual return toward the initial responses. The possibility to generate adaptive changes in the robot's behavior opens the way to using the neuro-robotic interface for studying the transformations induced in the brain tissue by long and short- term modifications of synaptic properties. This system offers the possibility of substituting the actual brain tissue with a computational model of its neurons and its connections. The comparison of biological adaptive changes with their simulated counterparts may provide us with new means to directly investigate the computational properties of synaptic plasticity.

This work has attracted a worldwide attention from a broad range of media, including the New Scientist, the New York Times, the Washington Post, the BBC, De Welt, Canadian Broadcasting System, ZDF German television. But perhaps an even greater significance has the fact that our abstract about this system at the 2000 annual meeting of the Society for Neuroscience was selected among the few (out of 13,000) that appeared in the Annual Meeting Press Book

CONCLUSIONS:

The AASERT award has provided an extremely valuable complement of the parent grant whose purpose was to combine the study of physiological mechanisms in the spinal cord with the development of artificial systems based on analogous mechanisms. The research under the AASERT award allowed the PI to develop a novel and successful line of research, aimed at the integration of living neural tissue with artificial devices. This goal has been accomplished and the first prototype of a hybrid system operating with a closed sensory-motor loop has been created and utilized for investigating the structure of the neural connections and the mechanisms of synaptic plasticity. A central element in the AASERT funded research has been the interdisciplinary training of a Mechanical Engineering student. Dr. Bernard Reger has completed his PhD requirements by defending an outstanding dissertation, whose title is, by itself, a clear demonstration of multidisciplinary research. Dr. Reger is currently involved in research activities with the Department of Defense.

SIGNIFICANCE:

The goal of the AASERT proposal was to explore a novel direction that had been opened by the parent project.

This new research activity provided a fertile ground for multidisciplinary graduate training in an area that is at the boundary between neuroscience, robotics and mechanical engineering.

The development of a hybrid system composed of a robotic device controlled by living neurons has two broad implications. On one hand, the use of neural tissue in a control system is the prototype of a computational architecture
that exploits some of the most distinctive features of biological information processing. Among these features is the ability of the nervous system to compensate for unexpected changes in operating conditions. In the long term, this research may lead to the development of new prosthetic and teleoperated devices based on the direct coupling of neural signals with the controlled apparatus.

On the other hand, the use of a robotic system in connection with a neural system in-vitro provides an effective and flexible instrument for testing hypotheses on the cellular mechanisms of learning. Current knowledge of these mechanisms indicates that the excitability of neurons may be altered by past experience. The hybrid system developed in thid proposal provides a new tool for understanding these mechanisms by effectively "programming" the brain tissue to generated a repertoire of robot behaviors in response to the presentation of a light source.

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